

CLAIMS

That which is claimed is:

1. A composition, comprising:
a pharmaceutically acceptable excipient; and
bacteria with altered DNA adenine methylase activity which altered DNA adenine methylase activity renders the bacteria non-pathogenic.
2. The composition of claim 1, wherein the bacteria are altered by an artificially engineered change in the bacteria's genome.
3. The composition of claim 2, wherein the change in the bacteria's genome is a change selected from the groups consisting of a deletion, an insertion and a mutation of a native sequence.
4. The composition of claim 1, wherein the bacteria are altered by a heterologous nucleotide.
5. The composition of claim 4, wherein the heterologous nucleotide is operatively inserted into a plasmid and expresses DNA adenine methylase.
6. The composition of claim 1, wherein the pathogenic bacteria are selected from the group consisting of *Escherichia*, *Vibrio*, *Yersinia* and *Salmonella*.

7. The composition of claim 6, wherein the pathogenic bacteria are a salmonella bacteria selected from the group consisting of *S. typhimurium*, *S. enteritidis*, *S. typhi*, *S. abortus-ovi*, *S. abortus-equi*, *S. dublin*, *S. gallinarum*, and *S. pullorum*.

8. The composition of claim 6, wherein the pathogenic bacteria are *E. coli*.

9. The composition of claim 6, wherein the bacteria are *V. cholerae*.

10. The composition of claim 6, wherein the bacteria are *Y. psuedotuberculosis*.

11. The composition of claim 1, wherein the bacteria are selected from the group consisting of *Shigella*, *Haemophilus*, *Bordetella*, *Neisseria*, *Pasteurella* and *Treponema*.

12. The composition of claim 1, wherein the bacteria are selected from the group consisting of *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus somnus*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mannheimia haemolytica*.

13. The composition of claim 1, wherein the bacteria are *Haemophilus*.

14. The composition of claim 1, further comprising an adjuvant.

15. An immunogenic composition, comprising:

a pharmaceutically acceptable excipient; and

live bacteria, said bacteria comprising altered DNA adenine methylase (Dam) activity wherein the altered activity reduces virulence relative to the bacteria with wild-type Dam activity.

16. The immunogenic composition of claim 15, wherein the Dam activity is altered by a heterologous nucleotide.

17. The immunogenic composition of claim 15, wherein the Dam activity is altered by a mutation in the bacteria's genome which mutation alters a gene involved in expressing Dam in a manner selected from the group consisting of reduced expression, no expression, overexpression, expression of a form of Dam altered from Dam native to the bacteria.

18. An attenuated strain of a pathogenic bacteria, said bacteria containing a mutation which alters Dam activity such that the bacteria are attenuated.

19. The attenuated strain of claim 18, wherein the mutation reduces Dam activity.

20. The attenuated strain of claim 18, wherein the mutation eliminates Dam activity.

21. The attenuated strain of claim 18, wherein the mutation is a deletion in a *dam* gene.

22. The attenuated strain of claim 18, wherein the mutation causes an increase in expression of Dam.

23. The attenuated strain of claim 18, wherein the bacteria is *Haemophilus*.

24. The attenuated strain of claim 18, wherein the bacteria are selected from the group consisting of: *Salmonella enterica* serovars, *E. coli*, *Non Typable Haemophilus influenza*, *Streptococcus pneumoniae*, *Helicobacter pylori*, *Shigella* spp., *Vibrio cholerae*, *Yersinia* spp., *Neisseria meningitidis*, *Porphyromonas gingivalis*, and *Legionella pneumophila*.

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25. The attenuated strain of claim 18, wherein the bacteria are selected from the group consisting of *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus somnus*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mannheimia haemolytica*.

26. A method, comprising the steps of:

administering to a subject capable of generating an immune response a composition comprising a pharmaceutically acceptable excipient an immunogenic dose of altered bacteria with altered DNA adenine methylase (Dam) activity which bacteria are attenuated; and

allowing the composition to remain in the subject for a time and under conditions to allow the subject to generate an immune response to the bacteria and produce antibodies specific to the bacteria.

27. The method of claim 26, wherein the antibodies generated are IgG type antibodies.

28. The method of claim 27, wherein the IgG antibodies are highly specific for an antigen of the bacteria.

29. The method of claim 26, wherein the bacteria remain in the subject under conditions and for a period of time sufficient to allow for B cells of the subject to undergo isotype switching and further for the B cells to undergo clonal expansion.

30. The method of claim 29, wherein an amount of antibodies produced by the subject exceeds 150% of an amount of antibodies which would be produced by the subject administered unaltered bacteria in amount equivalent to the immunogenic dose of altered bacteria.

31. The method of claim 26, wherein the bacteria are selected from the group consisting of *Escherichia*, *Vibrio*, *Yersinia* and *Salmonella*.

32. The method of claim 26, wherein the bacteria are *Haemophilus*.

33. A method of eliciting an immune response in an individual, comprising:

administering an immunogenic composition to an individual in an amount sufficient to elicit an immune response wherein the composition comprises a pharmaceutically acceptable carrier and a bacteria comprising a genome characterized by a mutation altering DNA adenine methylase (Dam) activity such that the bacteria is attenuated;

allowing the composition to remain in the individual for a time and under conditions to allow the individual to generate an immune response.

34. The method of claim 33, wherein the bacteria are *Haemophilus*.